Scope of vignette:
- authorised products (with marketing authorisation)
- decision process about routine use (and not individual requests for reimbursement)
- submissions for P&R made by manufacturers

Green= related to/any special considerations for OMPs/UOMPs

Bulgaria	**Standard HTA process (non-orphan drugs)**
Overview of health system and P&R/HTA process	Tax based health system [1] The marketing authorization holder submits an application for pricing and HTA at the National Council of Prices and Reimbursement of medicinal products (NCPR). The entire procedure is according to the ORDINANCE ON THE CONDITIONS, RULES AND PROCEDURE FOR REGULATING ANDREGISTRATION OF THE PRICES OF MEDICINAL PRODUCTS, last Update State Gasette 26, March 29, 2019 (Pricing Regulation). Regulation 9 on HTA, which was the legal HTA provision from 2016 until March 31, 2019 was repealed. The HTA activities were transferred from the National Centre for Public Health and Analyses to the NCPR. The Ministry of Health, the National Health Insurance Fund and the NCPR can initiate a health technology assessment. This initiative was newly introduced in April 2019, according to the Pricing Regulation where the HTA Regulation 9 from 2015 was repealed. [1] The National Center of Public Health and Analyses (NCPHA), a structure within the national healthcare system, was responsible for various activities, including HTA from December, 2015 until the end of March, 2019. [2] Since April 1, 2019, the NCPR is in charge of HTA in Bulgaria. A working committee on HTA within the NCPR advises the NCPR whether or not to include drugs on a positive list [1,2]. Since April 1, 2019, the pricing, reimbursement and HTA process is under auspices of the NCPR. There is a Committee on rare diseases, which makes a proposal to the Ministry of Health for inclusion of specific rare disease onto a List of Rare Diseases for Bulgaria (so called 'List'). Only treatments for rare diseases included on the List can be reimbursed, based on Regulation 16 from July 30, 2014. For inpatient reimbursement, the manager of the health establishment suggests to the director of the NCPHA potential designated expert centers for each rare disease. After the director's approval and inclusion in Annex 2 of the positive drug list, the product could be used for treatment in that particular hospital. For outpatient reimbursement, the medicinal product should be placed on the List of rare diseases for Bulgaria, on the Positive Drug List- Annex 1, and on the Drug List of the Health Insurance Fund.

Bulgaria	Standard HTA process (non-orphan drugs)
Differentiation of rare disease treatments in the P&R system	EMA orphan designation
Eligible medicines	New medicinal products with new international non-propriety and marketing authorization. [1] An OMP has the possibility to be reimbursed when the orphan disease is included on the List of rare diseases set up by the Ministry of Health in Bulgaria, and on the Positive Drug List after HTA.
Process	For HTA of OMPs, information is to be submitted regarding the efficacy and therapeutic effectiveness, and according to the new Guideline (Annex 6, point 5) of the Pricing and Reimbursement Ordinance from April 1, 2019. Details under 'appraisal framework'. Reference HTA countries for Bulgaria are UK, France, Germany, and Sweden, where just one of the HTAs should be positive before submission. 1. The HTA Working committee conducts a preliminary evaluation at the NCPR 2. A draft HTA report created by the Working committee is submitted to the NCPR. 3. A decision about the draft report should be made within 180 days by the NCPR [5]
Disease specific expert input (e.g. clinicians or patients in any stage of the process)	In order to support its activities, the NCPR sets up a different Working Committee for each new medicine (Committee includes physicians, pharmacists, economists, and representatives from the Ministry of Health or National Health Insurance Fund). During the decision making process, the Working Committee holds sessions. There is a Committee on rare diseases, which makes a proposal to the Ministry of Health for inclusion of specific rare disease onto a List of rare diseases for Bulgaria.
Key domains in assessment	Clinical effectiveness Cost-effectiveness Budget impact Other [4, 5]

Bulgaria	**Standard HTA process (non-orphan drugs)**
Evidentiary requirements	RCTs are preferred, and non-RCTs of treatment effects can provide secondary evidence The following evidentiary requirements are outlined according to Annex № 6, Art 35, items 3 and 6 of the Pricing Regulation: • Criteria, methods of identification, selection and databases that ensure the inclusion of all relevant randomized trials in the clinical evaluation • Strategy for the selection of clinical trials • The main objective is to identify all randomized trials that compare the new technology with the main alternative • If direct randomized comparisons are not found, randomized trials that will allow indirect comparisons should be sought. If it is not possible to make indirect comparisons, a search for non-randomized trials should be conducted • Any application of indirect comparisons and the inclusion of non-randomized trials should be justified • The recommended databases, which can be used to identify the tests of the evaluated health technology, are the following: PubMed, Cochrane Library, Clinical Trials gov., EU Clinical Trials Register
PROMs	Measures of HRQoL may be used.
Appraisal framework	Criteria for efficacy and therapeutic effectiveness: (a) An assessment of the therapeutic benefit of the medicinal product; (b) Prolonging life expectancy; (c) Improving the quality of life; (d) Additional therapeutic benefits; (e) Reducing complications from the underlying disease; (f) Patient convenience; (g) The effectiveness of the medicinal product associated with the specific formulation of and route of administration Criteria for pharmaco-economic indicators: (a) Costs of therapy with the medicinal product; (b) A comparison of the cost of therapy with the alternatives available; (c) Cost-performance ratio; (d) An economic assessment of the additional benefits; (e) An analysis of the budgetary impact on the basis of the expected number of patients; According to Annex 6, point 5 of the Pricing and Reimbursement, as amended in the April, 2019 Ordinance: The HTA of orphan drugs should meet the following additional criteria: 1. Information regarding efficacy and therapeutic efficacy 2. Submission for a specific period of time not longer than a year of additional evidence of the benefits of applying the medicinal product

Bulgaria	Standard HTA process (non-orphan drugs)
	3. Submission of Markov model for following-up the course of the disease 4.Assessment on the basis of severity and burden of the rare condition, availability of an alternative, and expenses covered by the patient if the medicinal product is not reimbursed 5. Moral and ethical considerations 6. Pharmacoeconomic evaluation and total budget impact shall be submitted for orphan medicinal products which bring big social benefits, which are not cost-effective and their use is indicated for serious conditions for which no alternative therapy exists 7. Summaries and reports from other HTA authorities/institutions for the health system benefits 8.The used literature should be provided and listed - published statements in the different countries. 9. Literature
Reimbursement decision	Decision is yes (add to Positive Drug list) or no (do not add to Positive Drug list)
Pricing process	Set in Chapter IV of the Pricing Regulation, with the reference to EU member states. All medicinal products on the Positive Drug List should provide annually mandatory discounts and 10 % clawback to the National Health Insurance Fund, as an obligation to be covered by public funds. That payback is within 3 years contract.
Managed entry agreements	- Confidential discount with finalised contract between MAH and National Health Insurance Fund or MoH before placing the medicinal product in the Positive Drug List. [1] - Budget cap
Main challenges in appraising medicines for rare diseases (tick all that apply)	X Lack of good quality clinical data – according to the published literature X Lack of real world data ☐ Introducing value for money ☐ Monitoring treatment efficacy ☐ Managing budget impact ☐ Lack of criteria/transparency of OMP P&R processes ☐ Making arrangements to work for all stakeholders ☐ Lack of long-term meaningful outcomes X Other: Lack of published HTA final statements according to templates of all products; Lack of registers of different diseases
Impact of special processes	---

Bulgaria	Standard HTA process (non-orphan drugs)
Proposed policy change	Last changes March 2019, in force as of April 1, 2019. On June 5, 2019, software was officially launched to monitor the effect of therapy on medicinal products with international non-proprietary name included in the Positive Drug List where HTA is not cost effective or lack of effectiveness data. The decision for therapy monitoring is included in the official document for inclusion the medicinal product in the Positive Drug List. Monitoring of the effect of therapy with medicinal products is carried out by medical institutions for hospital care and medical institutions under art. 5, para. 1, art. 10, item 3, 3a, 3b and 6 of the Medical Institutions Act, in which there are structures on the profile of the disease. In the course of monitoring the effect of therapy, the healthcare establishment (the hospital) will collect the information for each specific medicinal product and provide it to the NCPR on a daily basis by automatic transfer from the hospital information system. The data provided to the NCPR by the hospital information systems are relevant to the specified conditions and criteria for monitoring the effect of therapy with innovative medicinal products, and the information will be completely anonymised (containing personal information about the particular patient). The NCPR is publishing a list with medicinal products for monitoring the therapy. [3]
Joint initiatives	
SOURCES	
1	RULES AND PROCEDURE FOR REGULATING ANDREGISTRATION OF THE PRICES OF MEDICINAL PRODUCTS, published St. Gasette 40 from 30 April 2013 last Update State Gasette 26, 29 of March 2019 https://www.ncpr.bg/bg/нормативни-актове/българско-законодателство/наредби.html
2	Regulation 9 (repealed) http://ncpha.government.bg/index.php?option=com_content&view=article&id=1346:hta-commision-4&catid=358&Itemid=638&lang=bg
3	Monitoring of the effect of therapy of medicinal products with a new international non-proprietary name https://www.ncpr.bg/bg/ценообразуване-и-реимбурсиране/проследяване-на-ефекта-от-терапията/41-ценообразуване-и-реимбурсиране/409-актуално-до-02-05-2019-г.html
4	State of Health in the EU, Bulgaria Health country profile https://ec.europa.eu/health/sites/health/files/state/docs/chp_bulgaria_english.pdf
5	Ministry of Health ,National Centre for Public Health and Analyses http://ncpha.government.bg/index.php?lang=en

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This vignette was compiled based on information provided by country experts and desk research. The information provided may be incomplete or contain inaccuracies. If you have any comments or updates, please email us at the following email addresses:

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